

Replace the second full paragraph on page 4 (lines 17-24) with the following new

paragraph rewritten in clean form:

B2
Any of the fibronectin type III domain-containing proteins described herein may be formulated as part of a fusion protein (for example, a fusion protein which further includes an immunoglobulin F_c domain, a complement protein, a toxin protein, or an albumin protein). In addition, any of the fibronectin type III domain proteins may be covalently bound to a nucleic acid (for example, an RNA), and the nucleic acid may encode the protein. Moreover, the protein may be a multimer, or, particularly if it lacks an integrin-binding motif, it may be formulated in a physiologically-acceptable carrier.

Replace the final partial paragraph on page 4 (line 25) with the following new

partial paragraph rewritten in clean form:

B3
The present invention also features proteins that include a

Replace the fourth paragraph on page 11 (lines 10-14) with the following new

paragraph rewritten in clean form:

B4
FIGURE 5 is a photograph showing the structural similarities between a ¹⁰Fn3 domain and 15 related proteins, including fibronectins, tenascins, collagens, and undulin. In this photograph, the regions are labeled as follows: constant, dark blue; conserved, light blue; neutral, white; variable, red; and RGD integrin-binding motif (variable), yellow.

Replace the fifth paragraph on page 11 (lines 15-19) with the following new

paragraph rewritten in clean form:

B5
FIGURE 6 is a photograph showing space filling models of fibronectin III modules 9 and 10, in each of two different orientations. The two modules and the integrin binding loop (RGD) are labeled. In this figure, blue indicates positively charged residues, red indicates negatively charged residues, and white indicates

BS
ENCHOL

uncharged residues.

Replace the fourth paragraph on page 13 (lines 20-24) with the following new

paragraph rewritten in clean form:

B6

The antibody mimics of the present invention are based on the structure of a fibronectin module of type III (Fn3), a common domain found in mammalian blood and structural proteins. This domain occurs more than 400 times in the protein sequence database and has been estimated to occur in 2% of the proteins sequenced to date, including fibronectins, tenascin, intracellular cytoskeletal

Replace the second partial paragraph on page 19 (lines 14-24) with the following

new partial paragraph rewritten in clean form:

B7

The antibody mimics described herein may be used in any technique for evolving new or improved binding proteins. In one particular example, the target of binding is immobilized on a solid support, such as a column resin or microtiter plate well, and the target contacted with a library of candidate scaffold-based binding proteins. Such a library may consist of ¹⁰Fn3 clones constructed from the wild type ¹⁰Fn3 scaffold through randomization of the sequence and/or the length of the ¹⁰Fn3 CDR-like loops. If desired, this library may be an RNA-protein fusion library generated, for example, by the techniques described in Szostak et al., U.S.S.N. 09/007,005, now U.S. Patent No. 6,258,558 B1, and 09/247,190, now U.S. Patent No. 6,261,804 B1; Szostak et al., WO98/31700; and Roberts & Szostak, Proc. Natl. Acad. Sci. USA (1997) vol. 94, p. 12297-12302.

Alternatively, it may be a DNA-protein library (for example, as described in

Replace the first partial paragraph on page 20 (lines 1-9) with the following new

partial paragraph rewritten in clean form:

B8

Lohse, DNA-Protein Fusions and Uses Thereof, U.S.S.N. 60/110,549, filed December 2, 1998 and 09/453,190, filed December 2, 1999). The fusion library is incubated with the immobilized target, the support is washed to remove non-specific binders, and the tightest binders are eluted under very stringent

B8
conclude

conditions and subjected to PCR to recover the sequence information or to create a new library of binders which may be used to repeat the selection process, with or without further mutagenesis of the sequence. A number of rounds of selection may be performed until binders of sufficient affinity for the antigen are obtained.

Replace the last paragraph on page 24 (lines 18-20) with the following new paragraph rewritten in clean form:

B9

Unispl-s (splint oligonucleotide used to ligate mRNA to the puromycin-containing linker, described by Roberts et al, 1997, supra):
5'-TTTTTTTTNAGCGGATGC-3' (SEQ ID NO: 13)

Replace the second paragraph on page 25 (lines 10-22) with the following new paragraph rewritten in clean form:

B10

Next, each of the double-stranded fragments was transformed into a RNA-protein fusion (PROfusion™) using the technique developed by Szostak et al., U.S.S.N. 09/007,005, now U.S. Patent No. 6,258,558 B1, and U.S.S.N. 09/247,190, now U.S. Patent No. 6,261,804 B1; Szostak et al., WO98/31700; and Roberts & Szostak, Proc. Natl. Acad. Sci. USA (1997) vol. 94, p. 12297-12302. Briefly, the fragments were transcribed using an Ambion *in vitro* transcription kit, MEGAshortscript (Ambion, Austin, TX), and the resulting mRNA was gel-purified and ligated to a DNA-puromycin linker using DNA ligase. The mRNA-DNA-puromycin molecule was then translated using the Ambion rabbit reticulocyte lysate-based translation kit. The resulting mRNA-DNA-puromycin-protein PROfusion™ was purified using Oligo(dT) cellulose, and a complementary DNA strand was synthesized using reverse transcriptase and the RT primers described above (Unisplint-S or flagASA), following the manufacturer's instructions.

Replace the first partial paragraph on page 27 (lines 1-3) with the following new partial paragraph rewritten in clean form:

B11

from the master library following the general procedure described in Szostak et al.,